

- 1 1. A method of identifying a therapeutic target, the method comprising the steps of:
 - 2 (a) measuring protein or RNA levels of at least one component of an isolated mRNA
 - 3 ribonucleoprotein (mRNP) complex in a first sample enriched for a cell comprising a first
 - 4 phenotype; and
- 5 (b) comparing the levels determined in step (a) to the levels of the protein or RNA levels
- 6 of the component in a second sample enriched for a cell comprising a second phenotype,
- 7 wherein if the levels of the component in the first sample are different from the levels of
- 8 the component in the second sample, the component, a nucleic acid that encodes the component,
- 9 or a protein encoded by the component is a potential therapeutic target for the treatment of a
- 10 disease.
- 1 2. The method of claim 1, wherein the cell comprising the first phenotype is selected from
- 2 the group consisting of a mature adipocyte, a preadipocyte, pancreatic beta cell, a hepatocyte, a
- 3 skeletal muscle cell, and a cardiac muscle cell.
- 1 3. The method of claim 1, wherein the cell comprising the first phenotype is a mature
- 2 adipocyte and the cell comprising the second phenotype is a preadipocyte.
- 1 4. The method of claim 1, wherein the first phenotype is a disease related to glucose or lipid
- 2 metabolism and the second phenotype is a normal phenotype.
- 1 5. The method of claim 1, wherein the first phenotype is selected from the group consisting
- 2 of obesity, diabetes, hypoglycemia, glucotoxicity, lipidotoxicity, insulin-resistance,
- 3 hyperlipidemia, and lipodystrophy.
- 1 6. The method of claim 1, wherein the component is selected from the group consisting of
- 2 an RNA binding protein, an RNA, and an mRNP-associated protein.
- 1 7. The method of claim 1, the method further comprising the step of:
 - 2 (c) treating the sample in step (a) with an agent prior to measuring the protein or RNA
 - 3 levels of the component, wherein the agent alters the levels of at least one component of a
 - 4 glucose metabolic or a lipid metabolic pathway.

- 1 8. The method of claim 7, wherein the agent is selected from the group consisting of insulin,
2 glucose, insulin-like growth factor-1 (IGF-1), a β-adrenergic agonist, glucose, glucagon-like
3 peptide-1 (GLP-1), fatty acid, a peroxisome proliferator activated receptor (PPAR) ligand, and
4 insulin-like growth factor 2 (IGF-2).
- 1 9. The method of claim 7, wherein the agent is a test therapeutic.
- 1 10. The method of claim 7, wherein the agent is selected from the group consisting of a
2 nucleic acid, a protein, a peptide, or a small molecule.
- 1 11. The method of claim 1 or 7, further comprising the step of isolating the component, a
2 nucleic acid encoding the component, or a protein encoded by the component.
- 1 12. The method of claim 1, wherein the component is Polypyrimidine Tract Binding Protein.
- 1 13. The method of claim 1, wherein the RNA binding protein is selected from the group
2 consisting of the RNA binding proteins identified in Figure 10 to Figure 22.
- 1 14. The method of claim 1, wherein the component comprises a tag.
- 1 15. The method of claim 1, wherein the component is an mRNA that encodes a protein
2 selected from the group consisting of a kinase, a transporter, a phosphatase, channel protein, a
3 protease, a receptor, a transcription factor, and a transferase.
- 1 16. The method of claim 1, wherein the component is selected from the group consisting of
2 3-phosphoinositide dependent protein kinase-1, nuclear ubiquitous casein kinase 2, neural
3 receptor protein-tyrosine kinase, MAP-kinase activating death domain, AMP-activated protein
4 kinase beta-2 regulatory subunit, calcium/calmodulin-dependent protein kinase IV, Protein
5 kinase C beta, adenylate kinase 3, mitogen activated protein kinase kinase 5, 6-phosphofructo-2-
6 kinase/fructose-2,6-bisphosphatase 2, phosphatidylinositol 4-kinase, Glucokinase, glycogen
7 synthase kinase 3 beta, phosphorylase kinase (gamma 2, testis), protein tyrosine phosphatase
8 (non-receptor type 1), protein tyrosine phosphatase (non-receptor type 5), inositol
9 polyphosphate-5-phosphatase D, Protein tyrosine phosphatase (receptor-type, zeta polypeptide),
10 dual specificity phosphatase 6, protein tyrosine phosphatase (non-receptor type 12), glucose-6-
11 phosphatase (catalytic), 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 2, proton gated
12 cation channel DRASIC, Sodium channel (nonvoltage-gated 1, alpha (epithelial)), calcium

13 channel (voltage-dependent, alpha2/delta subunit 1), Potassium inwardly-rectifying (channel,
14 subfamily J, member 6), potassium channel regulator 1, calcium channel (voltage-dependent, T
15 type, alpha 1G subunit), cyclic nucleotide-gated cation channel, amiloride-sensitive cation
16 channel 1, potassium inwardly-rectifying channel J14, potassium large conductance calcium-
17 activated channel (subfamily M, alpha member 1), potassium voltage gated channel (Shab-
18 related subfamily, member 2), potassium channel subunit (Slack), potassium intermediate/small
19 conductance calcium-activated channel (subfamily N, member 1), Sodium channel (voltage-
20 gated, type V, alpha polypeptide), amiloride-sensitive cation channel 2 (neuronal), potassium
21 channel (subfamily K, member 6 (TWIK-2)), cation-chloride cotransporter 6, solute carrier
22 family 21 (organic anion transporter, member 12), amino acid transporter system A2,
23 peptide/histidine transporter, choline transporter, solute carrier family 31 (copper transporters,
24 member 1), solute carrier family 13 (sodium-dependent dicarboxylate transporter), solute carrier
25 family 2 (facilitated glucose transporter, member 13), solute carrier family 12 (potassium-
26 chloride transporter, member 5), Solute carrier family 6 (neurotransmitter transporter, serotonin,
27 member 4), Solute carrier family 2 A2 (glucose transporter, type 2), carboxypeptidase D,
28 ubiquitin specific protease 2, mast cell protease 1, proprotein convertase subtilisin / kexin, type
29 7, laminin receptor 1 (67kD, ribosomal protein SA), protein tyrosine phosphatase (non-receptor
30 type 1), calcium-sensing receptor, neural receptor protein-tyrosine kinase, glutamate receptor
31 (metabotropic 4), nuclear receptor subfamily 4 (group A, member 2), Neuropeptide Y5 receptor,
32 protein tyrosine phosphatase (non-receptor type 5), insulin-like growth factor 1 receptor, Protein
33 tyrosine phosphatase (receptor-type, zeta polypeptide), nuclear receptor subfamily 4 (group A,
34 member 3), glutamate receptor (metabotropic 1), Tumor necrosis factor receptor superfamily
35 (member 1a), insulin receptor, gamma-aminobutyric acid receptor associated protein, protein
36 tyrosine phosphatase, non-receptor type 12, cholinergic receptor (nicotinic, beta polypeptide 1),
37 olfactory receptor (U131), Gamma-aminobutyric acid receptor beta 2, glial cell line derived
38 neurotrophic factor family receptor alpha 1, Glycine receptor beta, glutamate receptor interacting
39 protein 2, adenylate cyclase activating polypeptide 1 receptor 1, asialoglycoprotein receptor 2,
40 adenosine A3 receptor, Fibroblast growth factor receptor 1, nuclear receptor binding factor 2,
41 purinergic receptor P2Y (G-protein coupled 1), nuclear receptor subfamily 1 (group H, member
42 4), peroxisome proliferator activator receptor(gamma), 5 hydroxytryptamine (serotonin) receptor
43 4, retinoid X receptor gamma, insulin receptor-related receptor, putative N-acetyltransferase
44 Camello 4, lecithin-retinol acyltransferase, Phenylethanolamine N-methyltransferase,
45 fucosyltransferase 2, Sialyltransferase 8 (GT3 alpha 2,8-sialyltransferase) C, UDP-

46 glucuronosyltransferase, alpha 1,3-fucosyltransferase Fuc-T (similar to mouse Fut4),
47 diacylglycerol O-acyltransferase 1, signal transducer and activator of transcription 3, ISL1
48 transcription factor (LIM/homeodomain), and oligodendrocyte transcription factor 1.

1 17. The method of claim 16, wherein the protein is encoded by a gene selected from the
2 group consisting of CNCG, CACNA2D1, KCNC3, and KCNB2.

1 18. A method for identifying a therapeutic target for the treatment of aberrant glucose
2 metabolism or lipid metabolism, the method comprising the steps of:

3 (a) measuring RNA or protein levels of at least one component of an isolated mRNP
4 complex in a first cell sample; and

5 (b) comparing RNA or protein levels determined in step (a) to the RNA or protein levels
6 of the component from a second cell sample,

7 wherein if the levels of the component in the first sample are different from the levels of the
8 component in the second sample, the component, a nucleic acid that encodes the component, or a
9 protein encoded by the component is a potential therapeutic target for the treatment of the
10 disease.

1 19. The method of claim 18, wherein the first cell sample is from an individual at risk of
2 having a disease or who has a disease and the second cell sample is from a normal or healthy
3 individual.

1 20. A method for identifying a therapeutic target related to the treatment of a disease, the
2 method comprising the steps of:

3 (a) measuring RNA or protein levels of at least one component of an isolated mRNP
4 complex in a sample that has been treated with an agent that alters the expression of a component
5 of a glucose metabolic or lipid metabolic pathway; and

6 (b) comparing RNA or protein levels determined in step (a) to the RNA or protein levels
7 of the component in an untreated control sample,

8 wherein if the levels of the component in the first sample are different from the levels of the
9 component in the second sample, the component, a nucleic acid that encodes the component, or a

10 protein encoded by the component is a potential therapeutic target for the treatment of the
11 disease.

1 21. A method for identifying a gene or gene product involved in a physiological pathway in a
2 cell, the method comprising the steps of:

3 a. isolating an mRNP complex comprising at least one component that participates
4 in a physiological pathway;

5 b. identifying at least one additional component of the isolated mRNP complex,
6 wherein the additional component is also involved in a physiological pathway.

1 22. The method of claim 21, wherein the physiological pathway comprises a metabolic
2 pathway or a regulatory pathway.

1 23. The method of claim 21, further comprising the step of confirming the activity of the
2 additional component by inhibiting the expression of the additional component in a cell and
3 determining the effect of the inhibition on metabolism.

1 24. The method of claim 23, wherein the inhibition step comprises inhibiting gene expression
2 of the additional component using an agent selected from the group consisting of an RNAi, an
3 antisense RNA, a ribozyme, and a PNA.

1 25. A method for identifying an agent that alters a physiological pathway, the method
2 comprising the steps of:

3 a. subjecting a cell sample to an agent;

4 b. isolating an mRNP complex comprising at least one component that participates
5 in a physiological pathway from the sample;

6 c. measuring the RNA or protein levels of at least one component of the isolated
7 mRNP complex,

8 d. comparing the RNA or protein levels of step (c) to the RNA or protein levels of
9 the component isolated from an untreated control sample,

10 wherein differential expression of the component in the agent-treated sample compared to the
11 untreated control sample is indicative that the agent regulates the physiological pathway.

1 26. The method of claim 25, wherein the agent interacts with or regulates a component of the
2 physiological pathway.

1 27. The method of claim 25, wherein the agent inhibits a physiological pathway.

1 28. The method of claim 25, wherein the agent enhances a physiological pathway.

1 29. The method of claim 25, wherein the physiological pathway is an insulin production
2 pathway or a lipogenesis pathway.

1 30. A method for identifying a protein that regulates glucose metabolism, the method
2 comprising the steps of:

3 a. measuring the expression in an isolated mRNP complex of at least one gene
4 product of a cell involved in glucose metabolism, wherein the gene product is selected from the
5 group consisting of an RNA binding protein, an mRNA associated with said RNA binding
6 protein, or an mRNP complex-associated protein;

7 b. treating the cell with an agent selected from the group consisting of insulin,
8 glucose, insulin-like growth factor-1 (IGF-1), a β -adrenergic agonist, glucose, glucagon-like
9 peptide-1 (GLP-1), fatty acid, a peroxisome proliferator activated receptor (PPAR) ligand, and
10 insulin-like growth factor 2 (IGF-2); and

11 c. measuring the expression of the gene product after treatment, wherein a
12 difference in expression of the gene product after treatment compared to expression of the gene
13 product before treatment is indicative that the protein regulates glucose metabolism.

1 31. A method for identifying an agent that regulates insulin production, the method
2 comprising the steps of:

3 a. contacting a cell involves in insulin production with a nucleic acid capable of
4 binding to at least one protein, wherein the protein is capable of binding to a 3' untranslated
5 region or a 5' untranslated region of a preproinsulin mRNA;

6 b. separating the nucleic acid from the protein; and

7 c. identifying the protein.

1 32. The method of claim 31, wherein the protein binds to a nucleic acid comprising a
2 sequence selected from the group consisting of 5'-gaauaaaaccuuugaaagagcacuac-3', 5'-
3 cccacacuacccuguccaccccucugcaaug-3', and 5'-
4 agccctaagtgaccagctacagtggaaaccatcagcaaggcaggtcattgttccaac-3'.

1 33. An mRNP complex-associated with at least one of glucose or lipid metabolism, wherein
2 the mRNP complex comprises a polypyrimidine tract binding (PTB) protein, and at least one
3 mRNA associated with the polypyrimidine tract binding protein.

1 34. A method for identifying a component of an mRNP complex, the method comprising the
2 steps of:

3 (a) transfecting a cell sample with a nucleic acid that inhibits the expression of an RNA
4 binding protein;

5 (b) isolating total RNA from the cell sample and from a control sample;

6 (c) identifying RNAs that have altered expression in the nucleic acid-transfected sample
7 compared to the control sample.

1 35. The method of any one of claims 1, 7, 18, and 20, wherein the disease is related to
2 aberrant glucose or lipid metabolism.

1 36. The method of claim 21 or 25, wherein the physiological pathway comprises a glucose or
2 lipid metabolic pathway.

1 37. The method of any one of claims 1, 17, 20, 25, and 30, wherein at least one of said
2 measuring and said comparing steps comprises the use of an array.